Macula Retinal Vasculitis and Choroiditis Associated with Granulomatosis with Polyangiitis

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Abstract

Purpose: To report a case series of two cases of granulomatosis with polyangiitis, previously known as Wegener granulomatosis, which developed macular necrosis, not previously associated with granulomatosis with polyangiitis, healed with fibrosis, despite aggressive immune-modulating therapy and good control of systemic disease.

Methods: Case series of two cases with observation of treatment progress.

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Results: The results reported the progress of response to treatment in the two cases, which resulted in the final outcome of fibrosis in the macula region, despite being on aggressive immune-modulating therapy and good systemic control.

Conclusion: Granulomatosis with polyangiitis can be associated with macular necrosis leading to fibrosis, unresponsive to immune-modulating therapy.

A significant proportion of granulomatosis with polyangiitis (GPA), previously known as Wegener granulomatosis, cases are associated with ocular complications, mainly orbital inflammation, peripheral keratitis, and scleritis. Less common ocular complications include retinitis, uveitis, retinal vascular occlusions, and exudative retinal detachment. We report a case series of two cases of GPA, which developed macular necrosis, not previously associated with GPA, healed with fibrosis, despite aggressive immune-modulating therapy (IMT) and good control of systemic disease.

Key words: granulomatosis with polyangiitis; retinal vasculitis; choroiditis; macula; necrosis

Materials and Methods

Case Series

Case 1

A 53-year-old white woman was diagnosed with GPA based on pulmonary mass lesion, hematuria, and elevated quantitative serum anti-proteinase 3 antibodies (cANCA) of 80 U/mL (normal < 2.4 U/mL). She was started on oral cyclophosphamide and prednisone, which resulted in resolution of the pulmonary mass lesion and hematuria. However, she developed painless visual loss in her left eye over 1 month with presenting visual acuity of counting fingers at 1 foot. The right eye was unaffected. Ocular examination of left eye revealed fine keratic precipitates in the cornea, with 1+ cells in the anterior chamber and 1+ vitreous cells, and an elevated yellowish macular lesion (Figure 1).

Case 2

A 46-year-old white man was referred to the ophthalmology department by the inpatient neurology service. He had a 1-month history of a gradual and profound visual loss in the right eye, with a recent onset of visual disturbance in the left a few days before referral. He had been otherwise healthy until 18 months before the onset of visual symptoms when he developed multiple upper respiratory problems and sequential neurologic deficits, separated in time by several months, including frequent rhinitis, followed by otitis media with hearing loss, numerous nose bleeds, Bell's palsy, difficulty with balance, recurrent Bell's palsy, and finally, weakness and numbness of his left foot. Just before presentation, he developed left upper eyelid ptosis and left forehead numbness. He had lost 30 pounds over the course of the previous year despite having been on and off oral prednisone for the last 6 months.

On initial examination, his visual acuity was 20/200 right eye and 20/25 left eye, with a right relative afferent pupillary defect. He had ptosis on the left and was noted to have a saddle nose deformity. Dilated fundus examination revealed 0.5+ vitreous cells on the right, with a large subretinal lesion involving the entire macula with partial extension to the mid-periphery and a small exudative retinal detachment inferiorly. The left posterior pole showed 3 foci similar appearing white subretinal lesions (Figure 3).

Results

Case 1

Fundus fluorescein angiography showed capillary nonperfusion and retinal vascular leakage compatible with occlusive retinal vasculitis within the lesion. Owing to the striking clinical appearance, an opportunistic fungal was suspected. Cyclophosphamide was stopped and systemic amphotericin B was begun. Serologic testing for IgG and IgM antibodies against Toxoplasma gondii, Toxocara spp, Histoplasma capsulatum, Aspergillus spp, Candida spp, and Coccidioides immitis was negative. Over the next 10 days, despite systemic antifungal therapy, the lesion enlarged. The patient underwent immediate diagnostic pars plana vitrectomy, subretinal aspiration and biopsy, and intravitreal injections of amphotericin B 5 µg, vancomycin 1 mg, amikacin 400 µg, and clindamycin 300 µg. No intraocular

corticosteroids were given. Histopathologic evaluation, including Gram and Giemsa stains, of the biopsied material from the vitreous, subretinal space, and retina revealed macrophages, lymphocytes, and neutrophils with no evidence of fungi, bacteria, or protozoa. Polymerase chain reaction for toxoplasmosis, HSV, HSV2, and VZV and fungal and bacterial cultures were negative. The prednisone dosage was increased postoperatively to 60 mg daily and tapered over 3 months. One month after surgery, the patient developed a rhegmatogenous retinal detachment from a break at the posterior macular biopsy site with early proliferative vitreo-retinopathy requiring pars plana vitrectomy, scleral buckle, and silicone oil tamponade. The macular lesion became fibrotic with 3 months of the first surgery (Figure 2). Over the next 12 months, the patient received a cumulative dose of 27 grams of cyclophosphamide after which she was switched to azathioprine for 5 years and is now maintained on methotrexate with complete remission of GPA.

Case 2

The patient underwent magnetic resonance imaging, which revealed enlargement of the left lateral and superior rectus muscles, extensive sinus disease, and pachymeningitis. Biopsy of the left orbit revealed a lymphoplasmacytic infiltrate, focal chronic vasculitis with vessel wall disruption (Figure 4), and no evidence of monoclonality or lymphoma on flow cytometry or cytology. No fungal or bacterial elements were seen or present on culture.

The patient was started on 60 mg of prednisone effecting a dramatic improvement in the appearance of the subretinal lesions within 3 weeks (Figure 5).

Although the patient's cANCA was originally negative, the positive myeloperoxidase antibody together with the clinical features, pathologic findings, and response to therapy modified our final diagnostic impression to that of myeloperoxidase ANCA positive GPA. After rheumatologic consultation, the patient started on oral cyclophosphamide with a slow prednisone taper, pneumocystis prophylaxis, and has continued to improve. The subretinal lesions were noted to resolve with overlying retinal pigment

epithelial disturbances with a best-corrected visual acuity of 20/200 (right eye) and 20/20 (left eye) at his last follow-up visit.

Discussion

Ocular complications, mainly peripheral keratitis and scleritis, occur in 30%–60% of GPA cases.1–3 Retinal vasculitis in GPA is uncommon and responds to IMT.4,5 Our patient unfortunately developed unilateral macular granuloma, not previously reported to be associated with GPA, which progressed to macular fibrosis despite aggressive IMT and good control of systemic disease. The reasons as to why the vasculitic process leading to macular necrosis was not responsive to IMT remained unclear. However, this complication was not previously reported in GPA, and the treating clinician should accord intensive IMT treatment to patients with GPA who demonstrate any inflammatory ocular problems. In conclusion, GPA can be associated with macular necrosis leading to fibrosis, unresponsive to IMT.

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Figures

Fig. 1. Case 1, maculopathy at presentation.

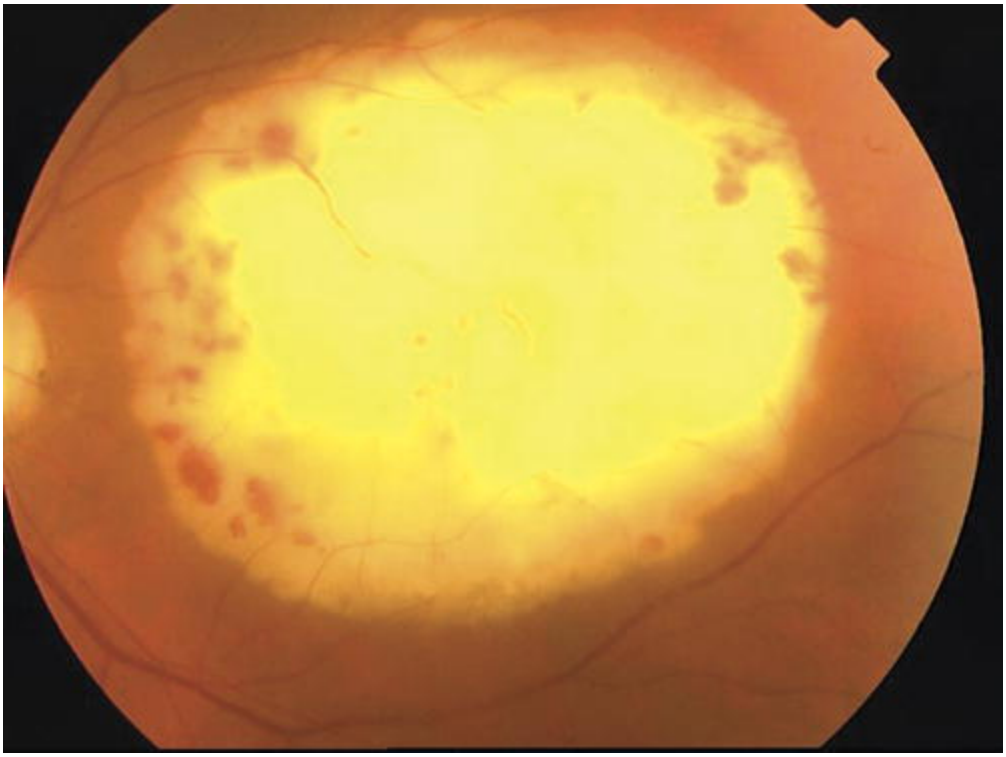

Fig. 2. Case 1, the fibrotic macula post treatment.

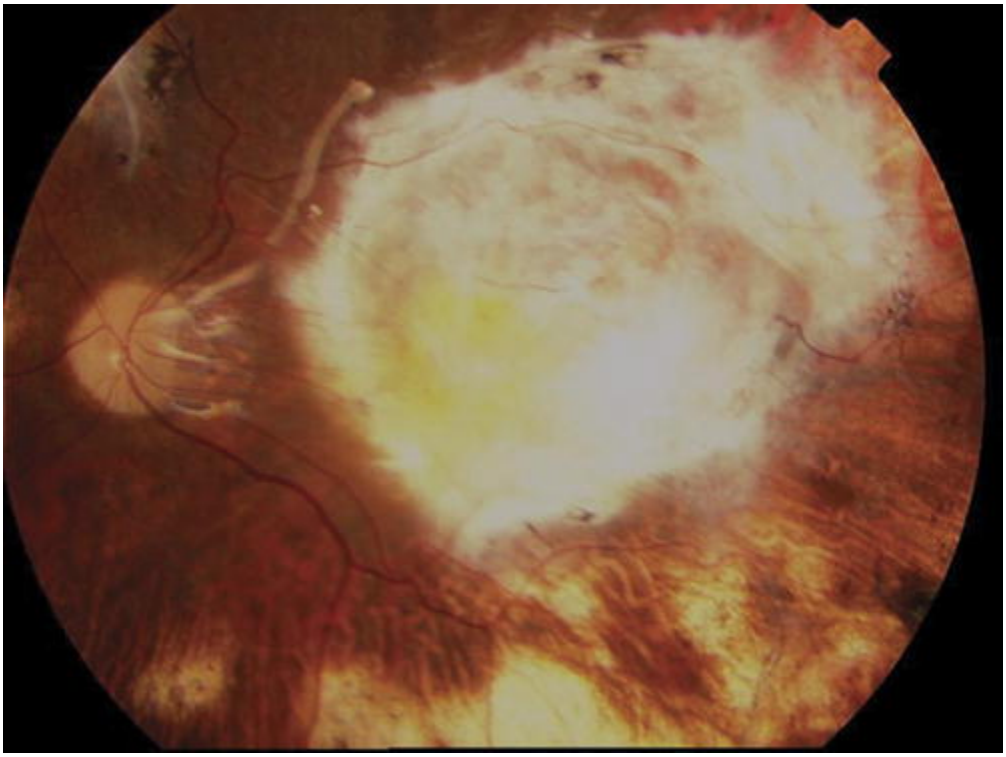

Fig. 3. Case 2, bilateral fundus at presentation.

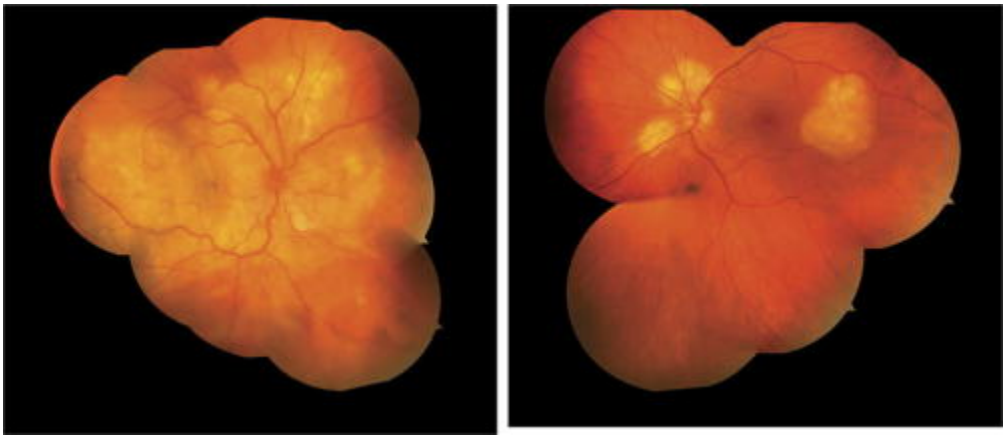

Fig. 4. Case 2, histology showing granulomatosis polyangiitis.

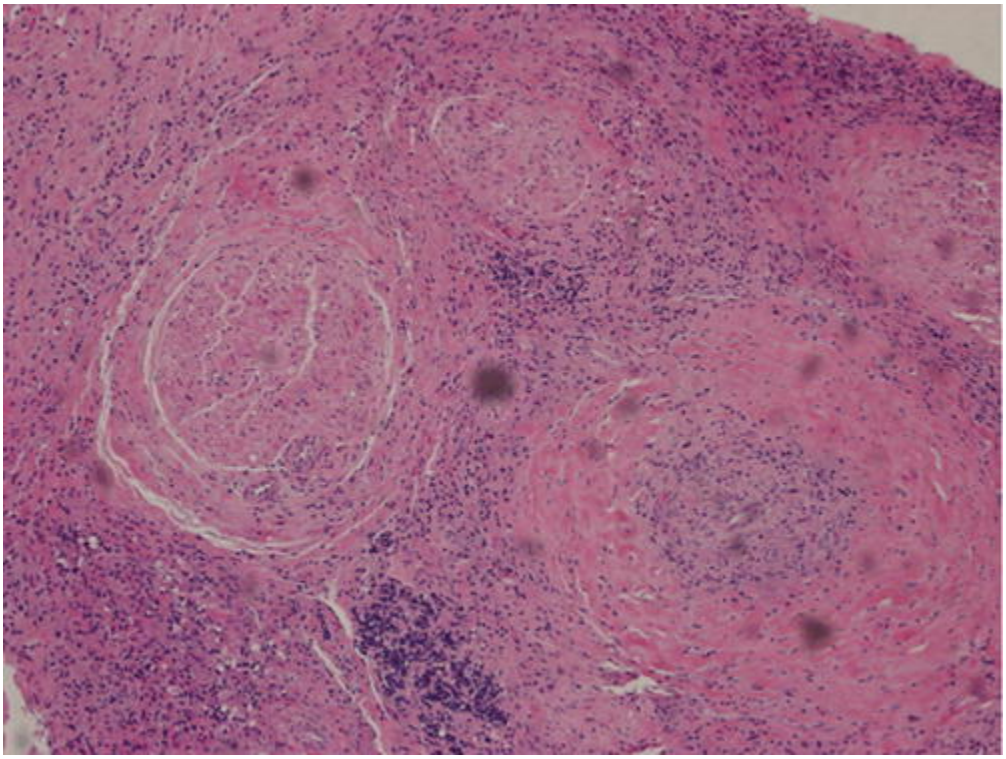

Fig. 5. Case 2, right and left fundus photographs, 22 days after beginning steroids.